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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/766,773	01/27/2004	Gregory J. LaRosa	1855.1052-028	3246

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EXAMINER	
BOESEN, AGNIESZKA	
ART UNIT	PAPER NUMBER
1648	
MAIL DATE	DELIVERY MODE
03/12/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/766,773	LAROSA ET AL.	
	Examiner	Art Unit	
	Agnieszka Boesen	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 December 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *54,55 and 57-77* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *54,55,57-74,76 and 77* is/are allowed.

6)☒ Claim(s) *75* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *1/20/2008*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The Amendment filed December 12, 2007 in response to the Office Action of August 6, 2007 is acknowledged and has been entered. Claims 54 and 55 have been amended. Claims 36-52 have been canceled. New claims 59-77 have been added. Claims 54, 55, and 57-77 are pending.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Rejection of claims 36-52 under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement **is moot** because Applicant canceled the claims.

Rejection of claims 54, 55, 57, and 58 under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement **is withdrawn** in view of Applicant's amendment.

New Rejection

New claim 75 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contain subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, have been described in In re Wands, 8 USPQ2d 1400 (Fed. Cir. 1988). Among these factors are: 1) scope or breadth of the claims; 2) nature of the invention; 3) relative level of skill possessed by one of ordinary skill in the art; 4) state of, or

the amount of knowledge in, the prior art; 5) level or degree of predictability, or a lack thereof, in the art; 6) amount of guidance or direction provided by the inventor; 7) presence or absence of working examples; and 8) quantity of experimentation required to make and use the claimed invention based upon the content of the supporting disclosure. When the above factors are weighed, it is the Examiner's position that one skilled in the art could not practice the invention without undue experimentation.

Claims are drawn to a method of treating a CCR2-mediated disorder in a patient comprising administering to the patient an effective amount of a humanized immunoglobulin or antigen-binding fragment thereof having binding specificity for CCR2. The constant region of the immunoglobulin or portion thereof is mutated to minimize binding to Fc receptors, the ability to fix complement or both.

The claim is rejected for lack of enablement, because the present specification does not provide sufficient support for the claimed mutated constant region or the portion of the constant region, wherein the mutation minimizes the binding of the Fc portion of the antibody to the Fc receptor or wherein the mutation minimizes the ability of the antibody to bind or fix complement. The claims broadly encompass ant type of mutation at any amino acid residues within the constant region of the antibody of the present invention. In support of the present claim Applicants generally discuss mutating the constant region of the antibody and refer to a number of references that should provide guidance with respect to making mutations resulting in minimizing the binding of the Fc portion of the antibody to the Fc receptors and to complement:

[0078] "The portion of the humanized immunoglobulin or immunoglobulin chain which is of human origin (the human portion) can be derived from any suitable human immunoglobulin or immunoglobulin chain. For example, a human constant region or portion thereof, if present, can be derived from the .kappa. or .lambda. light chains, and/or the .gamma. (e.g., .gamma.1,

.gamma.2, .gamma.3, .gamma.4), .mu., .alpha. (e.g., .alpha.1, .alpha.2), .delta. or .epsilon. heavy chains of human antibodies, including allelic variants. A particular constant region (e.g., IgG1), variant or portions thereof can be selected in order to tailor effector function. For example, **a mutated constant region (variant) can be incorporated into a fusion protein to minimize binding to Fc receptors and/or ability to fix complement (see e.g., Winter et al., GB 2,209,757 B; Morrison et al., WO 89/07142; Morgan et al., WO 94/29351, Dec. 22, 1994).**"

The specification does not provide working examples containing guidance regarding any specific mutations within the heavy chain constant region of the antibody that result in decreased binding of the Fc portion of the antibody to the Fc receptor or decreased ability of the antibody to fix complement. Without such guidance the skilled artisan would be required to conduct an undue amount of experimentation in order to determine which particular mutations within the heavy chain constant region would result in a decreased binding of the antibody Fc portion to its Fc receptor. It is acknowledged that mutations altering the binding of the constant region of the antibody have been done in the art, as evidenced by the references cited in Applicant's specification (see [0078] above). However making the mutations within the heavy constant region of the antibody of the present invention, wherein the mutations must result in a particular function would have been undue experimentation. The present specification does not provide any guidance with regard to which specific amino acids and at what positions should be mutated to result in decreased ability of the antibody to bind Fc receptors. Any random mutations of the constant region of the antibody could result in even higher binding affinity of the antibody Fc portion to the Fc receptors. Thus one would be required to conduct an undue amount of experimentation to test each and every candidate mutation to see which mutation result in decreased binding affinity of the antibody's constant region to the Fc receptor. This is because each and every constant region of an antibody would be expected to comprise a distinct

sequence. Therefore mutation experiments and testing the function of the mutations would have to be performed for the constant region of an antibody of the present invention.

Therefore considering the amount of experimentation that would be required in order to determine which particular mutations in the constant region of the present antibody could result in decreased binding of the antibody to the Fc receptors, and considering the lack of working examples in the specification, it is the position of the Office that Applicants have not provided sufficient enablement for the present claim.

Conclusion

SEQ ID NO: 12 and 17 are free of prior art of record. Claims 54, 55, 57-74, 76, and 77 are allowable.

Applicant's amendment necessitated the new ground of rejections presented in this Office action. Thus, **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Agnieszka Boesen whose telephone number is 571-272-8035. The examiner can normally be reached on Monday – Friday from 9:00 AM to 5:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell can be reached on 571-272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Agnieszka Boesen, Ph.D./
Examiner, Art Unit 1648

/Stacy B Chen/
Primary Examiner, Art Unit 1648